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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,443	EATON ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

This action is in response to papers filed 12 December 2005 in which no claims were amended, no claims were canceled, and no claims were added.

1. The previous rejections under the judicially created doctrine of obviousness-type double patenting are withdrawn in view of Applicant's Terminal Disclaimer, filed 12 December 2005 and approved 13December 2005.

2. The previous rejections under 35 U.S.C. 102(e) are withdrawn in view of the declarations submitted under 37 C.F.R. 1.132 and received 21 December 2005.

3. The previous rejections under 35 U.S.C. 103(a)not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are deemed moot.

4. Claims 28-39 are under currently prosecution.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 28 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993).

Regarding claim 28, Ellington et al teach the method of obtaining single-stranded DNA molecules capable of ligand binding that are isolated via selection and amplification in vitro (Abstract, lines 1-4). In addition, Ellington et al teach that nucleic acid aptamers may be new catalysts for chemical transformations that are analogous to catalytic antibodies (page 852, column 2, last paragraph). Ellington et al do not specifically teach the use of the Diels-Alder reaction.

However, Hilvert et al teach the use of a catalytic antibody to perform a Diels-Alder reaction (Abstract, lines 1-10). In addition, Hilvert et al teach that it would be beneficial to find a specific catalyst for a Diels-Alder reaction (column 5, lines 15-17).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free*

reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67).

Regarding claim 32, the method of claim 28 is discussed above. Ellington et al also teach the use of DNA oligomers having a region of conserved sequences (e.g., defined primer-binding sites; page 850, column 1, paragraph 2, lines 2-3) and a region of randomized sequences (page 850, column 1, paragraph 2, lines 1-2).

Regarding claim 33, the method of claim 28 is discussed above. Ellington et al teach the use of single-stranded DNA (page 850, column 1, paragraph 2, lines 4-6), and that the methods are similar to those used for RNA (Abstract, lines 1-4).

Regarding claims 34 and 35, the method of claim 28 is discussed above. Ellington also teaches that different single-stranded DNA oligomers can be selected to fold into specific ligand-binding structures (Title).

It would therefore have been obvious to a person of ordinary skill in the art at the time the inventions were claimed that single-stranded nucleic acid oligomers can be selected and amplified to specifically bind any discrete molecule; thus it is irrelevant whether the first reactant is a diene (claim 34) or a dieneophile (claim 35), as Ellington et al teaches that a nucleic acid could be selected to bind either one.

2. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152,

issued 4 May 1993) as applied to claim 28 above, and further in view of Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459).

Regarding claim 29, the method of claim 28 is discussed above. Neither Ellington nor Hilvert teach the use of linker groups.

However, Woo et al teach the use of psoralen probes that are tethered to oligonucleotides (first paragraph, lines 1-3). Woo et al also teach that "the degree to which chemical reactivity can be spatially focused on the target stand and the chemical transformations that can be achieved are of general interest (page 5458, column 1, lines 2-4)."

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The tethering technology of Woo et al would provide a reasonable expectation of successfully probing the degree to which chemical reactivity could be focused on the oligonucleotide (page 5458, column 1, lines 2-4).

3. Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No

5,208,152, issued 4 May 1993) and Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459) as applied to claim 29 above, and in further view of Cload et al (J. Am. Chem. Soc., 1993, 115, pp 5005-5014) as defined by Jolly (Modern Inorganic Chemistry, 1984, McGraw Hill).

Regarding claim 30, the method of claim 29 is discussed above. Neither Ellington et al, Hilvert et al, nor Woo teach the use of linker groups having a size in the range of 10 to 1000 Angstroms.

However, Cload et al teach the use of oligonucleotide probes tethered with a neutral polyethylene glycol linker (page 5006, column 1, paragraph 2, lines 4-6). Cload et al also teach that the linker is designed to minimize possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6). Finally, the average single bond lengths as described by Jolly (e.g., a C-C bond length of 1.54 Angstroms; Tables 3.5 and 3.6, page 52) clearly establish the length of the linker taught by Cload et al as being between 10 and 1000 Angstroms.

It would therefore have been obvious to one of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The tethering technology of Woo et al would provide a reasonable

expectation of successfully probing the degree to which chemical reactivity could be focused on the oligonucleotide (page 5458, column 1, lines 2-4), in particular given the teaching of Cload et al that the tether will minimize possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6).

Regarding claim 31, the method of claim 30 is described above. Cload et al also teach the use of polyethylene glycol-based linkers with the expected benefit of minimizing electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6).

4. Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in further view of Verdine (PCT International Publication Number WO 93/14108, published 22 July 1993).

Regarding claim 36, the method of claim 28 is discussed above. Neither Ellington nor Hilvert teach the attachment of functional groups.

However, Verdine teaches the attachment of functional groups (e.g., multidentate ligands, page 10, line 32) including substituted thiols and substituted carboxylic acids (page 11) to nucleic acids (page 7, lines 12-13 and Figure 1). Verdine also teaches that said functional groups can particularly be used to design and synthesize molecules which specifically bind a desired DNA sequence (page 8, lines 1-5).

It would therefore have been obvious to one of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The attachment of functional groups as taught by Verdine would provide the additional expected benefit of aiding in the design of "sequence-specific or site-specific DNA binding molecules (Verdine, page 8, lines 1-5).

Regarding claim 37, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a ribose position of said nucleic acid (e.g., at the sugar phosphate backbone; page 17, line 1).

Regarding claim 38, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a base of said nucleic acid (page 16, lines 31-32).

Regarding claim 39, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a phosphate position of said nucleic acid (e.g., at internucleotide phosphorous atoms; page 17, lines 1-2).

Response to Arguments

Applicant's arguments filed 12 December 2005 have been fully considered but they are not persuasive.

1. Applicant argues (Remarks, page 7, last paragraph) that with respect to instant claims 28 and 32-35, the method of Ellington et al does not teach a product library since the DNA sequences that are amplified bind to a specific target. However, Ellington et al specifically teach a method of producing a product library (e.g., pools of specific dye-binding DNA aptamers selected to bind each of three distinct dyes [CB, GR, and B4], said three distinct dyes thereby constituting a product library; Table 1).

2. Applicant reiterates (Remarks, page 7, last 2 lines) the Examiner's assertion that Ellington et al teach the use of nucleic acid ligands as catalysts for subsequent reactions. Ellington et al specifically teach an analogy between catalytic antibodies and nucleic acid aptamers to catalyze chemical transformations (page 852, column 2, last paragraph, and as cited above). Therefore, Ellington et al provide clear motivation to combine nucleic acid aptamers with chemical transformations demonstrated by catalytic antibodies.

3. Applicant reiterates (Remarks, page 8, lines 3-4) the Examiner's assertion that the Hilvert et al teach use of a catalytic antibody to perform a Diels-Alder reaction. Hilvert also specifically teach that it would be beneficial to find a specific catalyst for a Diels-

Alder reaction (column 5, lines 15-17, and as cited above) with the added benefit of significant rate enhancement (column 4, line 67). Therefore, Hilvert et al also provide clear motivation to perform a Diels-Alder reaction with a catalyst.

4. Applicant argues (Remarks, page 8, second paragraph) that the method as claimed requires coupling of the nucleic acid ligand to each first reactant. Hilvert et al specifically teach coupling of reactants to the catalyst (e.g., binding of the reactants to an antibody; column 4, lines 65-66). Ellington et al also teach coupling of substrates to the nucleic acid aptamers (e.g., DNAs bound to the affinity columns; page 850, column 2, paragraph 2, lines 3-5).

5. Applicant further argues (Remarks, page 8, second paragraph) that the instant claims do not require initial selection of the nucleic acid ligands. However, the invention as claimed is drawn to a method comprising the steps outlined in the instant claims, thereby allowing addition of steps not specifically listed in the claim.

6. Applicant also reiterates (Remarks, page 8, third paragraph) the Examiner's assertion that Ellington et al suggest that it is obvious to use their method to identify a catalyst for a chemical reaction.

7. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have combined the nucleic acid aptamers as taught by Ellington et al to obtain a catalyst for a Diels Alder reaction as taught by Hilvert et al. The ordinary artisan would have been motivated to combine the teachings of Ellington et al with those of Hilvert et al with the expected benefit of significant rate enhancement of the Diels Alder reaction as specifically taught by Hilvert et al (column 4, line 67). The combination of the teachings of Ellington et al in view of Hilvert et al thus satisfy each and every limitation of instant claims 28 and 32-35. Applicant's arguments with respect to claim 28 and 32-35 are therefore considered moot.

8. Applicant's remaining arguments reiterate Applicant's assertion that Ellington et al in view of Hilvert et al do not render the instant invention as set forth in independent claim 28 obvious. As such, Applicant therefore has not challenged the validity of the

additional cited references. The Examiner therefore maintains the previous rejections under 35 U.S.C. 103(a) in view of the Response to Arguments above.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert T. Crow
Examiner
Art Unit 1634

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